REMARKS/ARGUMENTS

With entry of this amendment, claims 1-6, 8-21 and 23-35 are pending in the above-identified application, claims 7 and 22 having been canceled. Claims 27, 28 and 32-35 have been withdrawn from consideration.

Claims 1, 12, 17, 25, 26 and 29 are amended. Support for the amendments to claims 1 and 17 is provided at, *e.g.*, page 4-5, paragraphs 16-17; page 7, paragraph 25; page 8, paragraph 26; page 23, Table 1; and in original claims 2-6. Claims 12 and 29 are amended to correct obvious typographical errors. Claim 26 is amended to depend from claim 17. No new matter is added by these amendments.

No amendment should be construed as an acquiescence of any rejection.

35 U.S.C. § 112, Second Paragraph

Applicants acknowledge the objection to the specification and rejections of claims 18 and 29 have been withdrawn.

Claim 29 stands rejected. Applicants believe that the instant objection is moot in view of the amendment to claim 29, in which the preamble was amended from "A composition" to "An isolated polypeptide." Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claim 29.

35 U.S.C. § 112, First Paragraph

Claims 1-11 and 13-22 stand rejected as allegedly failing to comply with the written description requirement. The Examiner alleges the function and structure of the polypeptides is not sufficiently described in the disclosure. The Examiner acknowledges that the specification describes polypeptides comprising a molecular weight between about 190 kD and about 100 kD and comprising SEQ ID NO: 1 and that have vWF protease activity (*see id.*). Applicants understand the Examiner's underlying concern to be that the specification allegedly does not describe the function of polypeptides having a molecular weight between about 190 kD and about 100 kD and comprising SEQ ID NO: 1 (*see* Office Action, page 3, lines 10-16.)

Applicants respectfully disagree. Initially, Applicants submit the Examiner's rejection presupposes that other proteins exist that lie within the recited size range and comprise SEQ ID NO: 1. Because the Examiner has not provided any evidence such proteins exist, Applicants submit the Examiner has not established a *prima facie* case.

Further, Applicants respectfully submit independent claim 1 recites, *inter alia*, a composition exhibiting vWF protease activity, and thus complies with the written description requirement. Dependent claims 2-6 and 8-16 comply with the written description requirement for the same reason.

With respect to independent claim 17, without acquiescing to the rejection, but to proceed with more compact prosecution of this case, Applicants amend claim 17 to recite an isolated polypeptide exhibiting vWF activity. Applicants submit claim 17, as amended, and dependent claims 18-21 (claim 22 having been canceled) comply with the written description requirement.

Applicants request the Examiner reconsider and withdraw the rejection of claims.

35 U.S.C. § 102(b)

Claims 1-26 and 29-31 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Furlan *et al.* (*Blood* 87:4223-4234, 1996). The Examiner acknowledges that Furlan *et al.* "do not particularly teach that the composition [having vWF protease activity] contains peptide chains that are between 190 and 100 kD, [e.g.] 180 kD, 170 kD, 160 kD, 120 kD, 110 kD." Instead, the Examiner contends "one skilled in the art can recognize in Fig. 7 of the article the bands corresponding to the enumerated molecular weights" by relying on a second reference, Gerritsen *et al.* (*Blood* 98:1654-1661, 2001).

"[A] prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is *necessarily present*, or inherent, in the single anticipating reference." *Schering Corporation v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1667 (Fed. Cir. 2003) (emphasis added). *See also* MPEP § 2112. Although recognition of the missing characteristic need not be present in the alleged prior art, a finding that the missing characteristic is necessarily present must be based on a proper

determination of the disclosure of the alleged prior art reference. *See id.* Inherency may not be established by mere possibilities or probabilities. *See, e.g., Mehl/Biophile Int'l Corp. v. Milgraum, M.D.*, 192 F.3d 1362, 1365, 52 USPQ2d 1303, 1305 (Fed. Cir. 1999). *See also* MPEP § 2112(IV).

Applicants respectfully disagree with the Examiner. As discussed in the response to the prior office action, Furlan *et al.* only teach that a 300 kD protein on an SDS-PAGE gel under non-reducing conditions coincided with vWF protease activity. Under reducing conditions, the strongest staining bands were associated with bands of 65 and 50 kD. Furlan *et al.* characterize the other proteins in Figure 7 as contaminants.

> Although the final product was purified about 10,000-fold, the protease was still ***contaminated by a number of nonidentified proteins***. The elution of the [vWF] proteolytic activity coincided with the appearance of a protein with an M_r of 300 kD. On reduction of disulfide bridges, the main polypeptide bands migrated in SDS-PAGE, with apparent M_r of 65 and 50 kD."

(*See* Furlan *et al.*, page 4232, first column, middle paragraph) (emphasis added).

Applicants submit the assertion that one skilled is the art would recognize in bands in Figure 7 of Furlan *et al.* that correspond to the vWF protease proteins disclosed by Gerritsen *et al.* is simply speculation. The mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish the thing is necessarily present. *See, e.g., Mehl/Biophile*, 192 F.3d at 1365, 52 USPQ2d at 1305.

Applicants submit a *prima facie* case has not been established because Furlan *et al.* and Gerritsen *et al.* use different purification methods. Furlan *et al.* use a purification procedure including:

> copper chelate chromatography;
> hydrophobic chromatography; and
> gel filtration chromatography.

In contrast, Gerritsen *et al.* use a purification procedure including:

> IgG-eTTPaffi-Gel® chromatography;

gel filtration chromatography;

protein G-Sepharose;

anion exchange with High Q Support®; and

Lentil-Lectin-Sepharose.

Unlike Furlan *et al.*, the first step of Gerritsen *et al.* is an immunoaffinity step using autoimmune serum which immunospecifically selects vWF-cp and certain other proteins. (*See* Gerritsen *et al.*, page 1656.) The additional steps remove contaminants, such as antibodies. Because the proteins are immunospecifically selected, they include vWF protease of different lengths. The purification method of Furlan *et al.* selects proteins based on other characteristics, including ability to bind to a copper chelation column, hydrophobicity and size. Therefore, because the purification methods and the protein characteristics used are different, Applicants submit the Examiner has not established that the vWF proteins of Gerritsen *et al.* will necessarily result by following the purification procedure of Furlan *et al.*

The proteins resulting from the purification methods of Furlan *et al.* and Gerritsen *et al.* are also different. Furlan *et al.* report major contaminating proteins having M_r of 450 kD, 200 kD, 180 kD and 130 kD in SDS-PAGE under non-reducing conditions. In contrast, the vWF protease proteins of Gerritsen *et al.* had M_r of 150 kD, 140 kD, 130 kD and 110 kD by SDS-PAGE under non-reducing conditions.

Furlan *et al.* further report that by SDS-PAGE under reducing conditions, only a small fraction of the total protein had a molecular weight greater than 80 kD (Furlan *et al.*, page 4228 (right column).) In contrast, the vWF protease proteins of Gerritsen *et al.* exhibit major bands greater than 80 kD in M_r. Applicants submit these dissimilarities in the resulting purified proteins are inconsistent with the Examiner's assertion.

In addition, Furlan *et al.* only reported that the vWF protease activity coincided with the 300 kD protein (under non-reducing conditions). Furlan *et al.* did not describe that vWF proteolytic activity coincided with any of the contaminants (*see* Furlan *et al.*, pages 4228 and 4232). Applicants submit that Furlan *et al.* would have noticed and/or checked for vWF proteolytic activity associated with other bands in the gels, and thus would have reported such

activities. The absence of such statements by Furlan *et al.* is inconsistent with the Examiner's assertion.

Further, even if the bands of Furlan *et al.* have the same M_r as the vWF protease proteins of Gerritsen *et al.*, Applicants submit such coincidence of size merely suggests a possibility that the bands of Furlan *et al.* "might" be vWF protease. Given the differences in purification procedures, the resulting proteins, and the large amount of contaminating proteins in the gels of Figure 7 of Furlan *et al.*, Applicants submit it is simply too speculative for the Examiner to reasonably assert that purification method will necessarily result in the vWF protease proteins of Gerritsen *et al.*

Applicants also disagree that SEQ ID NO: 1 and SEQ ID NO: 4 are inherent features of the bands described by Furlan *et al.* Again, because the purification methods are different, the resulting proteins are different, and the gels in Figure 7 of Furlan *et al.* include many contaminants, Applicants submit there is not sufficient evidence that the vWF protease proteins described by Gerritsen *et al.* are necessarily the same as the bands in Figure 7 of Furlan *et al.*

Finally, the Examiner stated a *prima facie* case of inherency has been established and then said the burden was on the Applicants to show novel or unobvious differences between the claimed compositions and the bands of Furlan *et al.* Applicants respectfully disagree. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied [reference]." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. Int. 1990) (emphasis original). *See also* MPEP § 2112(IV).

Applicants submit the only basis stated in the office action, that "one skilled in the art can recognize in Fig. 7 of the article the bands corresponding to the enumerated molecular weights" is not sufficient to reasonably support this rejection. Any alleged correlation between the bands of Figure 7 of Furlan *et al.* and the vWF protease proteins of Gerritsen *et al.* is too speculative, given the differences in purification methods, the differences in major resulting proteins, and the number of contaminants in Figure 7 of Furlan *et al.*, to support such an

assertion. Applicants therefore believe the Examiner has not established a proper *prima facie* case, and the burden has not shifted to Applicants to demonstrate otherwise.

Therefore, Applicants submit the claims are not anticipated by Furlan *et al.* Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

Dated: 9/20/04 By: Mol Sandbaken

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